Hypokalaemia: Bartter's syndrome or pseudo-Bartter's syndrome?[1]

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Summary: The difficulties in the diagnosis of hypokalaemia are often considerable. This paper reports three patients who presented with hypokalaemia. Investigations are described which may help to distinguish Bartter's syndrome from pseudo-Bartter's syndrome.

Introduction

Bartter's syndrome is often difficult to distinguish from pseudo-Bartter's syndrome (Gill 1980), a condition which may be caused by diuretic or laxative abuse. This paper describes investigations carried out on three patients who presented with hypokalaemia. The results of the investigations are discussed in relation to their ability to distinguish Bartter's syndrome from pseudo-Bartter's syndrome.

Case reports

Case 1 (Bartter's syndrome): A single 31-year-old nursery nurse presented with tetany. There was no past history of renal disease and no relevant family history. She denied taking diuretics or laxatives. On examination she appeared very apprehensive, anxious and tearful. Trousseau's sign was positive at 30 seconds. Blood pressure was 100/70 mmHg. Ultrasonography of the adrenal glands was normal. Urinalysis and creatinine clearance were normal. Screening of urine for frusemide and thiazides gave consistently negative results. Plasma calcium was 2.37 mmol/l and serum ionized calcium 1.10 mmol/l. Hypomagnesaemia was present (plasma magnesium 0.49 mmol/l; normal range 0.75–1.25). Plasma renin activity was 7.8 ng/ml/h supine (normal range 0.59–1.89) and 11.1 ng/ml/h erect (normal range 1.32–3.74). Plasma aldosterone was 174 pg/ml supine (normal range 35–115) and 393 pg/ml erect (normal range 110–350). The results of other investigations are shown in Table 1. The water-loading test and estimation of maximal free water clearance and distal fractional chloride reabsorption were carried out according to Solomon *et al.* (1982). Leukocyte sodium efflux rate constants were determined using a modification of the method described by Hilton & Patrick (1973).

Case 2 (diuretic abuse): A single 25-year-old seamstress complained of pain at the site of a previous cholecystectomy. She initially denied taking diuretics but subsequently, on being confronted with the results of urine analysis showing the presence of frusemide, did admit to the taking of 'water tablets' in order to lose weight. Her past medical history included periodic episodes of depression and a cholecystectomy one year earlier.

Examination showed an obese patient with a rather flat affect. Blood pressure was 100/70 mmHg. CAT scanning revealed normal appearance of the adrenal glands. Urinalysis and creatinine clearance were normal. Screening of urine gave consistently positive results for frusemide. Thyroid function tests were normal. Plasma cortisol was 410 mmol/l at midnight and 600 mmol/l at 8 am. Plasma calcium was 2.49 mmol/l. Hypomagnesaemia was

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Table 1. Results of investigations

	Electrolytes							Range urinary PGE_2 (ng/24 h)	Water loading test		Leukocyte sodium efflux rate constants (mg protein^{-1} h^{-1})	
	Plasma (mmol/l)				24 h urinary (mmol)				Free water clearance (ml/m)	Distal fractional chloride reabsorption	Oubain sensitive	Oubain insensitive
	Na^+	K^+	Cl^-	HCO_3^-	Na^+	K^+	Cl^-					
Case 1 (Bartter's syndrome)	138	1.8	97	28	224	75 (90)●	228	177–917	5.8	0.76	2.12	0.35
Case 2 (diuretic abuse)	137	2.2	92	31	242	123 (43)●	259	149–1023	5.2	0.87	2.27	0.97
Case 3 (laxative abuse)	139	2.9	100	25	10 (20)■	15	13 (27)■	338–903	5.6	0.97	0.98	0.15
Normal values (mean ± s.e. mean)								76–281[1]	9.2 ± 1.63[2]	0.84 ± 0.06[2]	2.95 ± 0.19 (n = 22)	0.66 ± 0.17 (n = 22)

●Spironolactone (100 mg/day) ■NaCl supplementation (100 mmol/day)
[1]Solomon *et al.* 1982; [2]Gill 1980

present (plasma magnesium 0.44 mmol/l). Plasma renin activity was 14.0 (supine) and 14.3 (erect) ng/ml/h. Plasma aldosterone was 184 (supine) and 583 (erect) pg/ml. The results of other investigations are shown in Table 1.

Case 3 (laxative abuse): A 44-year-old housewife complained of dyspnoea, central chest tightness on exertion and extreme fatigue. Her past medical history included several hospital admissions as a result of fainting attacks and a recent vaginal hysterectomy. Hypokalaemia was first discovered fifteen years earlier. Various estimations of plasma potassium over the years had given values in the range 1.5–3.8 mmol/l. She denied taking diuretics or laxatives. However, her husband stated that he had repeatedly found tins of Andrews Liver Salts in the home.

Examination showed a thin, anxious, easily agitated patient. Blood pressure was 110/70 mmHg and pulse rate was regular at 80/min. ECG showed no evidence of ischaemic change. Echocardiogram, chest X-ray and pulmonary function tests were normal. Attempts to carry out a stress ECG were abandoned when the patient developed severe dyspnoea. Urinalysis and creatinine clearance were normal. Screening of urine for thiazides and frusemide yielded consistently negative results. Total plasma calcium was 2.2 mmol/l. Plasma magnesium was 0.75 mmol/l; plasma renin activity was 13.1 ng/ml/h in both the supine and erect positions; plasma aldosterone 772 (supine) and 605 (erect) ng/ml/h. The results of other investigations are shown in Table 1. The use of potassium supplements quickly restored the plasma potassium to within the normal range.

Discussion

Three patients presented with hypokalaemia. The patient with pseudo-Bartter's syndrome as a consequence of diuretic abuse is clearly distinguished from the patient with Bartter's syndrome by (*a*) conservation of urinary potassium in response to spironolactone, and (*b*) the presence of frusemide in the urine. The patient with pseudo-Bartter's syndrome due to laxative abuse displayed marked urinary sparing of electrolytes which persisted during sodium chloride supplementation. This feature was not present in Bartter's syndrome or in pseudo-Bartter's syndrome (diuretic abuse) both of which appear to involve abnormal tubular function. However, the possibility exists that prolonged diuretic abuse will lead eventually to tubular damage and consequent wasting of electrolytes.

The cause of Bartter's syndrome is still controversial (Costello & Bourke 1983). Excess renal prostaglandin production has been suggested as an aetiological factor. However, all our patients showed variable levels of urinary PGE_2. It has been postulated that Bartter's syndrome arises from a defect in active chloride reabsorption in the ascending limb of the loop of Henle, resulting in decreased free water clearance and distal fractional chloride reabsorption (Gill *et al.* 1976). Our results suggest that measurement of free water clearance is not a useful distinguishing test but that a high distal fractional chloride reabsorption (> 0.95) may serve to separate laxative abuse (without tubular damage) from Bartter's syndrome or diuretic abuse. Some patients with Bartter's syndrome have been shown to have defects of membrane cation transport (Solomon *et al.* 1982).

The studies on our patients suggest that the apparent depression of the sodium-potassium pump may be secondary to hypokalaemia and not specific to Bartter's syndrome. The importance of a careful history and investigation of background is emphasized. In the case of suspected pseudo-Bartter's syndrome we stress the usefulness of the covert testing of urine for diuretics and the measurement of urinary electrolytes.

References

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